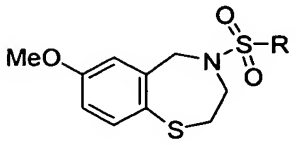
CLAIMS

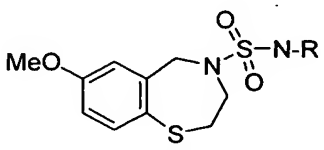
What is claimed is:

1. A compound having formula:



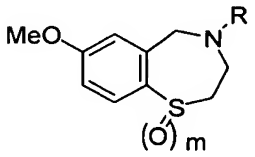
wherein R = aryl, alkenyl, $-(CH_2)_nNR'_2$, or $-(CH_2)_nSR'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl.

2. A compound having formula:



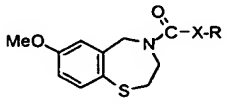
wherein R = aryl, alkyl, $-(CH_2)_nNR'_2$, or $-(CH_2)_nSR'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl.

3. A compound having formula:



wherein R = $CO(CH_2)_nXR'_2$, $SO_2(CH_2)_nXR'_2$, or $SO_2NH(CH_2)_nXR'_2$, and X = N or S, and n = 1, 2, or 3, and R' = alkyl or cycloalkyl; and wherein m = 1 or 2.

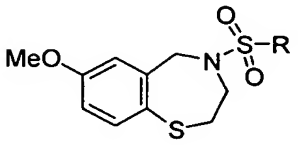
4. A compound having formula:



wherein R = aryl, alkyl, $-(CH_2)_nNR'_2$, $-(CH_2)_nSR'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl; and wherein X = NH or O.

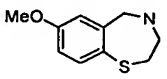
5. A compound selected from the group consisting of S7, S-20, S-25, S-27, and S36.

6. A method for the synthesis of a compound having formula:

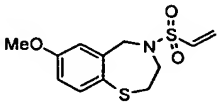


wherein R = aryl, alkenyl, alkyl, $-(CH_2)_nNR'_2$, or $-(CH_2)_nSR'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl, comprising the steps of:

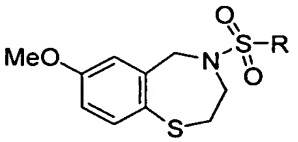
(a) treating a compound having formula:



with a sulfonyl chloride compound and a base, to form a compound having the formula:



(b) optionally, treating the compound formed in step (a) with a primary or secondary amine, to form a compound having formula:



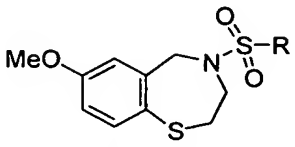
wherein R is as defined above.

7. The method of claim 6, wherein the sulfonyl chloride compound in step (a) is selected from the group consisting of alkylsulfonyl chloride and arylsulfonyl chloride.

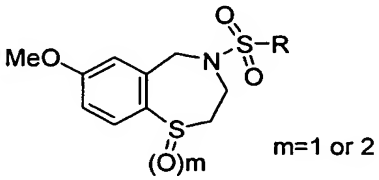
8. The method of claim 7, wherein the base in step (a) is Et_3N.

9. The method of claim 6, wherein the primary or secondary amine in step (b) is 4-benzylpiperidine.

10. The method of claim 6, further comprising the step of oxidizing the compound having formula:



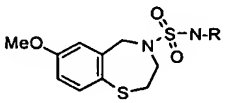
wherein R = aryl, alkenyl, alkyl, $-(CH_2)_nNR'_2$, or $-(CH_2)_nSR'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl, with an oxidizing agent, to form a compound having formula:



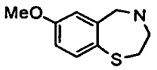
wherein R is as defined above, and wherein m = 1 or 2.

11. The method of claim 10, wherein the oxidizing agent is hydrogen peroxide.

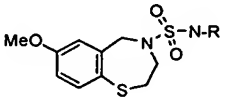
12. A method for the synthesis of a compound of having formula:



wherein R = aryl, alkyl, $-(CH_2)_nNR'_2$, or $-(CH_2)_nSR'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl, comprising the step of treating a compound having formula:



with a sulfuryl chloride and a primary or secondary amine, in the presence of a base, to form a compound having the formula:

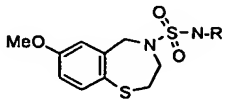


wherein R is as defined above.

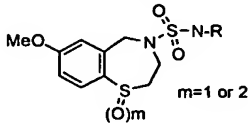
13. The method of claim 12, wherein the base is Et_3N.

14. The method of claim 12, wherein the primary or secondary amine is 1-piperonylpiperazine.

15. The method of claim 12, further comprising the step of oxidizing the compound having formula:

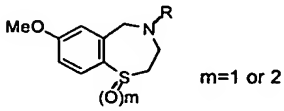


wherein R = aryl, alkyl, $-(CH_2)_nNR'_2$, or $-(CH_2)_nSR'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl, to form a compound having formula:

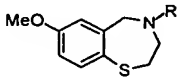


wherein R is as defined above, and wherein m = 1 or 2.

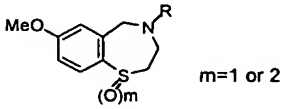
16. A method for the synthesis of a compound of having formula:



wherein R = $CO(CH_2)_nXR'_2$, $SO_2(CH_2)_nXR'_2$, or $SO_2NH(CH_2)_nXR'_2$, and X = N or S, and n = 1, 2, or 3, and R' = alkyl or cycloalkyl; and wherein m = 1 or 2, comprising the step of treating a compound having formula:



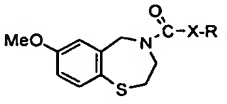
wherein R is as defined above, with an oxidizing agent, to form a compound having formula:



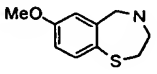
wherein R and m are as defined above.

17. The method of claim 16, wherein the oxidizing agent is hydrogen peroxide.

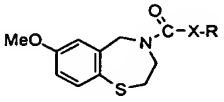
18. A method for the synthesis of a compound having formula:



wherein R = aryl, alkyl, $-(CH_2)_nNR'_2$, or $-(CH_2)_nSR'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl; and wherein X = NH or O, comprising the step of treating a compound having formula:



with a carbonyl chloride compound, in the presence of a base, and with a primary or secondary amine or an alcohol, to form a compound having the formula:



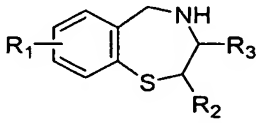
wherein R and X are as defined above.

19. The method of claim 18, wherein the carbonyl chloride compound is triphosgene.

20. The method of claim 18, wherein the base is Et_3N.

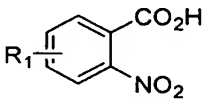
21. The method of claim 18, wherein the primary or secondary amine is 4-benzylpiperidine.

22. A method for the synthesis of 2, 3, 4, 5-tetrahydro-1,4-benzothiazepine compounds having formula:

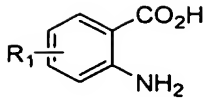


wherein R_1 = OR', SR', NR', alkyl, or halide, at position 2, 3, 4, or 5 on the phenyl ring, and R' = alkyl, aryl, or H; wherein R_2 = H, alkyl, or aryl; and wherein R_3 = H, alkyl, or aryl, comprising the steps of:

(a) treating a compound having formula:

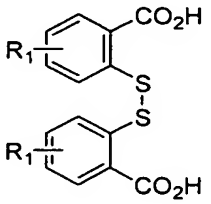


wherein R_1 is as defined above, with a reducing agent, in the presence of an optional catalyst, to form a compound having formula:



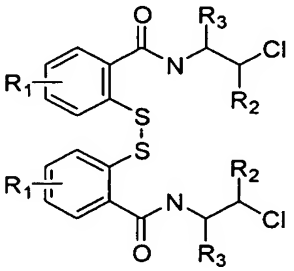
wherein R_1 is as defined above;

(b) treating the compound formed in step (a) with a diazotizing agent and a disulfide, to form a compound having formula:



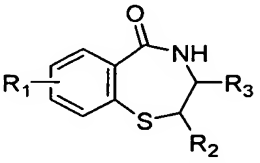
wherein R_1 is as defined above;

(c) treating the compound formed in step (b) with an activating agent and chloroethylamine, to form a compound having formula:



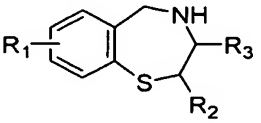
wherein R_1, R_2, and R_3 are as defined above;

(d) treating the compound formed in step (c) with a reducing agent and a base to form a compound having formula:



wherein R_1, R_2, and R_3 are as defined above; and

(e) treating the compound formed in step (d) with a reducing agent, to form a compound having formula:



wherein R_1, R_2, and R_3 are as defined above.

23. A method for identifying an agent that enhances binding of RyR2 and FKBP12.6, comprising the steps of:

(a) obtaining or generating a source of RyR2;

(b) exposing the RyR2 to FKBP12.6, in the presence of a candidate agent; and

(c) determining if the agent enhances the binding of RyR2 and FKBP12.6.

24. The method of claim 23, wherein the RyR2 is PKA-phosphorylated.

25. The method of claim 24, wherein the RyR2 is PKA-hyperphosphorylated.

26. The method of claim 23, wherein the RyR2 is immobilized to a solid phase.

27. The method of claim 26, wherein the solid phase is a plate or beads.

28. The method of claim 23, wherein the FKBP12.6 is radio-labeled.

29. The method of claim 28, wherein the FKBP12.6 is labeled with ^{32}S.

30. The method of claim 23, wherein enhanced binding of RyR2 and FKBP12.6 is detected using an FKBP12.6-binding agent.

31. The method of claim 30, wherein the FKBP12.6-binding agent is an anti-FKBP12.6 antibody.

32. An agent identified by the method of claim 23.

33. A method for identifying an agent for enhancing the binding of RyR2 and FKBP12.6, comprising the steps of:

(a) obtaining or generating a source of FKBP12.6;

(b) exposing the FKBP12.6 to RyR2, in the presence of a candidate agent; and

(c) determining if the agent enhances the binding of RyR2 and FKBP12.6.

34. The method of claim 33, wherein FKBP12.6 is immobilized to a solid phase.

35. The method of claim 34, wherein the solid phase is a plate or beads.

36. The method of claim 33, wherein RyR2 is PKA-phosphorylated.

37. The method of claim 36, wherein RyR2 is PKA-hyperphosphorylated.

38. The method of claim 33, wherein the RyR2 is radio-labeled.

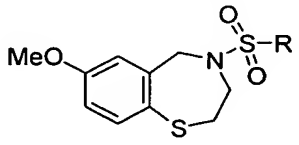
39. The method of claim 38, wherein the RyR2 is labeled with ^{32}P.

40. The method of claim 33, wherein enhanced binding of RyR2 and FKBP12.6 is detected using an RyR2-binding agent.

41. The method of claim 40, wherein the RyR2-binding agent is an anti-RyR2 antibody.

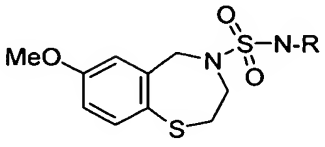
42. An agent identified by the method of claim 33.

43. A method for limiting or preventing a decrease in the level of RyR2-bound FKBP12.6 in a subject, comprising administering to the subject an amount of agent effective to limit or prevent a decrease in the level of RyR2-bound FKBP12.6 in the subject, wherein the agent is selected from the group consisting of:



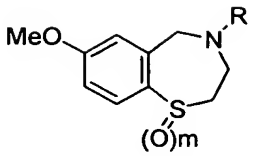
(a)

wherein R = aryl, alkenyl, alkyl, $-(CH_2)_nNR'_2$, or $-(CH_2)_nSR'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl;



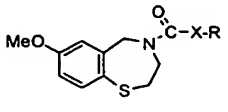
(b)

wherein R = aryl, alkyl, $-(CH_2)_nNR'_2$, or $-(CH_2)_nSR'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl;



(c)

wherein R = $CO(CH_2)_nXR'_2$, $SO_2(CH_2)_nXR'_2$, or $SO_2NH(CH_2)_nXR'_2$, and X = N or S, and n = 1, 2, or 3, and R' = alkyl or cycloalkyl; and wherein m = 1 or 2; and



(d)

wherein R = aryl, alkyl, $-(CH_2)_nNR'_2$, $-(CH_2)_nSR'$, and n = 0, 1, 2, or 3, and R' = alkyl or cycloalkyl; and wherein X = NH or O.

44. The method of claim 42, wherein the decrease in the level of RyR2-bound FKBP12.6 is limited or prevented in the subject by decreasing the level of phosphorylated RyR2 in the subject.

45. The method of claim 43, wherein the subject is a human.

46. The method of claim 43, wherein the subject has catecholaminergic polymorphic ventricular tachycardia (CPVT).

47. The method of claim 43, wherein the subject is a candidate for heart failure, atrial fibrillation, or exercise-induced cardiac arrhythmia.

48. The method of claim 43, wherein the amount of the agent effective to limit or prevent a decrease in the level of RyR2-bound FKBP12.6 in the subject is an amount of the agent effective to treat or prevent heart failure or atrial fibrillation.

49. The method of claim 43, wherein the amount of the agent effective to limit or prevent a decrease in the level of RyR2-bound FKBP12.6 in the subject is an amount of the agent effective to treat or prevent exercise-induced cardiac arrhythmia in the subject.

50. The method of claim 43, wherein the amount of the agent effective to limit or prevent a decrease in the level of RyR2-bound FKBP12.6 in the subject is an amount of the agent effective to prevent exercise-induced sudden cardiac death in the subject.